What is claimed is:

1. A MHC fusion complex comprising,

a MHC molecule that contains a peptide-binding groove, and

a presenting peptide covalently linked to the MHC peptide and positioned such that the presenting peptide can modulate the activity of a T cell.

2. A fusion complex of claim 1 wherein the MHC molecule is MHC class II.

3. A fusion complex of claim 2 wherein the presenting peptide is covalently linked to the N-terminus of the $\beta$ chain of the MHC protein.

4. A fusion complex of claim 2 wherein the presenting peptide is covalently linked to the $\alpha$ chain of the MHC protein.

5. A fusion complex of claim 2 wherein the presenting peptide contains from about 6 to 30 amino acids.

6. A fusion complex of claim 1 wherein the MHC molecule is MHC class I.

7. A fusion complex of claim 6 wherein the presenting peptide is covalently linked to the N-terminus of the $\alpha$ chain of the MHC protein.

8. A fusion complex of claim 7 wherein the presenting peptide contains about 6 to 15 amino acids.

9. A fusion complex of claims 1, 2 or 6 wherein a linker sequence is interposed between the MHC molecule and the presenting peptide.

10. A fusion complex of claim 2 wherein the MHC fusion complex does not contain the transmembrane and cytoplasmic domain of the MHC molecule, and is linked to a constant region of an immunoglobulin.

11. A fusion complex of claim 10 wherein $\alpha$ and $\beta$ chains of the fusion complex without the transmembrane and cytoplasmic domains are linked to immunoglobulin kappa and heavy chains, respectively.

12. A DNA construct coding for the fusion complex of claims 1 or 2.

13. A multivalent MHC fusion complex comprising two or more linked MHC fusion complexes of claim 1.

14. A method for identification of a peptide that can module the activity of T cells, comprising:

introducing into host cells cloning vectors that each contain DNA constructs that code for a MHC fusion complex of claim 1;

culturing the host cells under conditions suitable for expression of the MHC fusion complex; and

selecting host cells that express MHC fusion complex that modulate the activity of T cells.

(1988). The L243 monoclonal antibody is specific to a conformational epitope of the properly folded HLA-DR1 molecule [Gorga, J.C. et al. (1992) J. Biol. Chem. 262:16087-16094], and therefore would be preferred for purifying the biologically active MHC fusion complex.

Truncated MHC fusion complexes of the invention contain a MHC molecule that is sufficiently truncated so the MHC fusion complex can be secreted into culture medium after expression. Thus, a truncated MHC fusion complex will not include regions rich in hydrophobic residues, typically the transmembrane and cytoplasmic domains of the MHC molecule. Thus, for example, for a preferred truncated DR1 MHC molecule of the invention, preferably from about residues 199 to 237 of the $\beta$ chain and from about residues 193 to 230 of the $\alpha$ chain of the MHC molecule are not included in the truncated MHC fusion complex. See the examples which follow.

Multivalent MHC fusion complexes of the invention are preferred for a number of applications. The valence of a MHC-antigenic peptide complex influences the effect of the complex on T cell receptor(s). For example, activation of the 3DT52.5 T cell hybridomas requires a MHC-antigenic molecule that has been made multivalent. Monovalent, soluble MHC complexes are incapable of stimulating this T cell [McCluskey, J. et al. (1988) J. Immunology 141, 1451-1455]. Preferred multivalent MHC fusion complexes of the invention includes those linked to an immunoglobulin, e.g., IgG, IgM or $Fab'_2$. Chemically cross-linked MHC fusion complexes of the invention (for example cross-linked to dendrimers) are also suitable multivalent species. For example, the MHC fusion complex can be genetically modified by including sequences encoding

amino acid residues with chemically reactive side chains such as Cys or His. Such amino acids with chemically reactive side chains may be positioned in a variety of positions of a MHC fusion complex, preferably distal to the presenting peptide and binding domain of the MHC fusion complex. For example, the C-terminus of the $\beta$ chain of a MHC molecule distal from the presenting peptide suitably may contain such reactive amino acid(s). Suitable side chains can be used to chemically link two or more MHC fusion complexes to a suitable dendrimer particle to give a multivalent MHC fusion complex. Dendrimers are synthetic chemical polymers that can have any one of a number of different functional groups of their surface [Tomalia, D.A. (1993) Aldrichimica Acta 26:91:101]. Exemplary dendrimers for use in accordance with the

present invention include e.g. E9 starburst polyamine dendrimer and E9 combburst polyamine dendrimer, which can link cysteine residues.

It may be preferable to construct a single expression vector that expresses both chains of an MHC fusion complex of the invention, i.e. sequences that code for both the $\alpha$ and $\beta$ chains of an MHC fusion complex are each connected to a single expression vector. Such an expression vector may provide better results than where separate vectors are used for each chain of a MHC fusion complex, particularly where selection is difficult for cells into which the vector has been introduced. It also may be preferred to construct a single expression vector that codes for both chains of a MHC fusion complex as well as other agents, particularly a T cell costimulatory factor such as B7 or B7-2, i.e. sequences that code for both chains of an MHC fusion complex and sequence(s) that code for a costimulatory factor are each connected to a single expression

complex modulated T cell activation. For example, a decrease in IL-2 production of APC-stimulated T cells identifies those MHC fusion complexes that modulate activity of the T cells and suppress the immune responses. Alternatively, the in vitro assays can be employed to identify multivalent MHC fusion complexes of the invention described above, that contained presenting peptides that increase T cell responses.

In vivo assays also may be suitably employed to determine the ability of a MHC fusion complex of the invention to modulate the activity of T cells, including the ability to inhibit or inactivate T cell development. For example, an MHC fusion complex of the invention can be assayed for its ability to inhibit immunoglobulin class switching (i.e. IgM to IgG). See, e.g., Linsley, P.S. et al. (1992) Science 257:792-795. Such an assay is specifically described in Example 6 which follows.

Assays also may be employed to evaluate the potential use of a MHC complex of the invention for treatment of an immune disorder. For example, experimental allergic encephalomyelitis (EAE) is an autoimmune disease in mice and a recognized model for multiple sclerosis. A suitable mouse strain can be treated to develop EAE and then a MHC fusion complex of the invention administered and the animal evaluated to determine if EAE development is inhibited or prevented after administration of the MHC fusion complex. Such an assay is specifically described in Examples 8 and 11 which follow.

The ability of a MHC fusion complex of the invention to induce an immune response, including to provide vaccination against a targeted disorder, may be readily determined by an in vivo assay. For example, a

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2. A fusion complex of claim 1 wherein the MHC molecule is MHC class II.

3. A fusion complex of claim 2 wherein the presenting peptide is covalently linked to the N-terminus of the $\beta$ chain of the MHC protein.

4. A fusion complex of claim 2 wherein the presenting peptide is covalently linked to the $\alpha$ chain of the MHC protein.

5. A fusion complex of claim 2 wherein the presenting peptide contains from about 6 to 30 amino acids.

6. A fusion complex of claim 1 wherein the MHC molecule is MHC class I.

7. A fusion complex of claim 6 wherein the presenting peptide is covalently linked to the N-terminus of the $\alpha$ chain of the MHC protein.

8. A fusion complex of claim 7 wherein the presenting peptide contains about 6 to 15 amino acids.

9. A fusion complex of claims 1, 2 or 6 wherein a linker sequence is interposed between the MHC molecule and the presenting peptide.

10. A fusion complex of claim 1 wherein a linker sequence is interposed between the MHC molecule and the presenting peptide and the linker contains a cleavage site.

11. A fusion complex of claim 1 wherein a linker sequence is interposed between the MHC molecule and the presenting peptide and the linker sequence contains from 8 to about 12 amino acids.

12. A fusion complex of claim 2 wherein the MHC fusion complex does not contain the transmembrane and cytoplasmic domain of the MHC molecule, and is linked to a constant region of an immunoglobulin.

13. A fusion complex of claim 12 wherein $\alpha$ and $\beta$ chains of the fusion complex without the transmembrane and cytoplasmic domains are linked to immunoglobulin kappa and heavy chains, respectively.

14. A DNA construct coding for the fusion complex of claims 1 or 2.

15. A multivalent MHC fusion complex comprising two or more linked MHC fusion complexes of claim 1.

16. A method for identification of a peptide that can modulate the activity of T cells, comprising: